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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/853,524 | 05/10/2001 | Su-Chen Chang | 205032000420 | 6780 |

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| EXAMINER |
|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/853,524 | CHANG ET AL. | |
| | Examin r | Art Unit | |
| | Gailene R. Gabel | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Amendment Entry*

1. Applicant's amendment and response filed 4/21/03 in Paper No. 9 is acknowledged and has been entered. Claims 1-20 have been cancelled. Claims 21-33 have been added. Accordingly, claims 21-33 are pending.

### *Rejections Moot*

2. The rejections of claims 1-6 and 10-20 are now moot in light of Applicant's cancellation of the claims.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 21-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 26, 31, and 32 are indefinite in reciting, "gpIIbIIIa". Acronyms or abbreviations must be fully defined and recited at least one time in a set of claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In this case, the mode or mechanism of how adenosine is used to specifically prevent the diseases recited in claims 23 and 28 to enable claims 21 and 26, is described in the specification.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those of skill in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

*The nature of the invention*- the invention is directed to a method of preventing platelet membrane receptor protein gpIIbIIIa-associated disorders in a mammal, comprising thromboembolic disorders such as atherosclerosis, arteriosclerosis, acute myocardial infarction, angina, transient ischemic attack, stroke, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, and carotid endarterectomy, by

administering to the mammal an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa.

*The state of the prior art*- the prior art of record fails to disclose a method of preventing the platelet membrane receptor protein gpIIbIIIa-associated thromboembolic disorders in a mammal, by administering to the mammal an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa.

*The predictability or lack thereof in the art*- there is no predictability based on the instant specification that the claimed method of using adenosine will work in specifically and differentially preventing the platelet membrane receptor protein gpIIbIIIa-associated thromboembolic disorders in mammals.

*The amount of direction or guidance present*- the specification fails to provide any guidance to enable the claimed method to function in preventing the platelet membrane receptor protein gpIIbIIIa-associated thromboembolic disorders.

*The presence or absence of working examples*- There are no working examples that show that platelet membrane receptor protein gpIIbIIIa-associated thromboembolic disorders are prevented by administering to a mammal an effective amount of adenosine.

*The quantity of experimentation necessary*- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

*The relative skill of those in the art*-the level of skill in the art is high.

*The breadth of the claims*- as recited, the instant claims are directed to a method that is applicable for both treating and preventing platelet membrane receptor protein

gpIIbIIIa-associated thromboembolic disorders. As recited, the instant method of using adenosine will both treat and prevent thromboembolic disorders such as atherosclerosis, arteriosclerosis, acute myocardial infarction, angina, transient ischemic attack, stroke, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, and carotid endarterectomy, by administering to the mammal an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa.

The specification at page 3, lines 9-16 provides that adenosine is a well known compound as an antiarrhythmic, but has not been indicated for use in inhibiting platelet aggregation and thrombus formation. At page 7, Applicant has shown that by inhibiting platelet aggregation and thrombus formation, gpIIbIIIa-associated thromboembolic disorders can be treated by administering to a mammal an effective amount of adenosine. Examples 6 and 7 also provide an evaluation of the antithrombotic activity adenosine. However, nowhere in the specification provides a teaching of how such thromboembolic disorders are prevented by specific administration of an effective amount of adenosine to mammals. Prevention of certain disease states such as gpIIbIIIa-associated thromboembolic disorders requires that a certain amount of adenosine is administered to normal asymptomatic mammalian subjects to effectively inhibit activation of gpIIbIIIa to thus, prevent thromboembolic disorders which include atherosclerosis, arteriosclerosis, acute myocardial infarction, angina, transient ischemic attack, stroke, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, and carotid endarterectomy recited in claims 23 and 28. However, nowhere in the specification describes the mode or mechanism or dosage at which adenosine

can differentially and effectively prevent, as opposed to effectively treat these gpIIbIIIa-associated thromboembolic disorders. Based on Applicant's limited disclosure, one skilled in the art would not know how to prevent platelet membrane receptor protein gpIIbIIIa-associated disorders in a mammal by merely administering an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa to enable the method and composition in claims 23 and 26, without undue experimentation.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method of preventing platelet membrane receptor protein gpIIbIIIa-associated disorders in a mammal using adenosine, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work to differentially prevent all the thromboembolic disorders; 3) there is no proper guidance that shows effective prevention of the gpIIbIIIa-associated disorders in a mammal using adenosine, 4) the nature of the invention is a method of preventing platelet membrane receptor protein gpIIbIIIa-associated disorders in a mammal, comprising thromboembolic disorders such as atherosclerosis, arteriosclerosis, acute myocardial infarction, angina, transient ischemic attack, stroke, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, and carotid endarterectomy, by administering to the mammal an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that shows

differential prevention of gpIIbIIIa-associated thromboembolic disorders in a mammal, and lastly 7) the claims broadly recite a method of using adenosine to both treat and prevent thromboembolic disorders such as atherosclerosis, arteriosclerosis, acute myocardial infarction, angina, transient ischemic attack, stroke, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, and carotid endarterectomy, by administering to the mammal an amount of adenosine that is effective in inhibiting the activation of gpIIbIIIa, without specifically stating how this can be done without undue experimentation.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 21-30 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by Sollevi (US Patent 5,731,296).

The rejection of claims 21-30 as being inherently anticipated by Sollevi addresses only the "treatment" option of the claimed invention.

Sollevi discloses administering to human beings an effective amount of adenosine by continuous infusion for use in treating various disease conditions (see Abstract). Sollevi specifically reports that adenosine has a variety of biological effects whether it is endogenously or exogenously administered, including inhibition of platelet

aggregation (anti-aggregatory effect), antithrombotic effect (inhibit clot formation), vasodilation, peripheral and cardiovascular effects, and hypotensive activity. Accordingly, adenosine is administered for use in treating thromboembolic disorders such as hypertension, arterial thrombosis, ischemia, and peripheral vascular diseases (see column 1, lines 23-36, column 2, lines 39-64, column 3, lines 11-15, and column 20, lines 12-28). Adenosine is administered to a patient as a composition in any pharmaceutically acceptable carrier, i.e. diluent such as isotonic saline, or form (see column 3, lines 27-61). Sollevi also discloses administering adenosine in combination with another antithrombic such as heparin for the purpose of platelet protection during cardiopulmonary bypass (see Example VI).

While Sollevi is silent in teaching that adenosine is effective in inhibiting the activation of platelet membrane receptor protein gpIIbIIIa, the instant claims merely recite a newly discovered mechanism of adenosine, i.e. inhibits activation of gpIIbIIIa, for inhibiting platelet aggregation and thrombosis in the (known) method taught by Sollevi. The claim language is only a statement of purpose and intended result but the expression does not result in a manipulative difference of the method steps with that taught by Sollevi. Accordingly, newly discovered property and result of known processes and compositions directed to the same purpose are not patentable because such results are inherent.

6. Claims 21-25 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by Wang et al. (FASEB Journal 9 (3) : page A322 (1995)).

The rejection of claims 21-25 as being inherently anticipated by Wang et al. addresses only the "treatment" option of the claimed invention

Wang et al. teach that administration of adenosine has an antithrombotic effect in dogs as in vivo models of arterial thrombosis. Wang et al. further administer adenosine in combination with aspirin as antithrombotic.

Wang et al. is silent in teaching that adenosine is effective in inhibiting the activation of platelet membrane receptor protein gpIIbIIIa.

While Wang et al. is silent in teaching that adenosine is effective in inhibiting the activation of platelet membrane receptor protein gpIIbIIIa, the instant claims merely recite a newly discovered mechanism of adenosine, i.e. inhibits activation of gpIIbIIIa, for inhibiting thrombosis in the (known) method taught by Wang et al.. The claim language is only a statement of purpose and intended result but the expression does not result in a manipulative difference of the method steps with that taught by Wang et al. Accordingly, newly discovered property and result of known processes and compositions directed to the same purpose are not patentable because such results are inherent.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sollevi (US Patent 5,731,296) in view of Foster (4,444,879).

Sollevi has been discussed supra. Sollevi differs from the instant invention in failing to disclose incorporation of adenosine composition and pharmaceutically acceptable carrier into a kit format.

Foster et al. disclose reagents and containers (vials) in a kit format for use in an assay method (see column 15).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the adenosine, antithrombics, pharmaceutical carriers, and containers taught by Sollevi into a kit arrangement as taught by Foster et al. because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

***Response to Arguments***

8. Applicant's arguments filed 4/21/03 have been fully considered but they are not persuasive.

A) Applicant argues that the claims are not anticipated by Sollevi and Wang et al. nor are they rendered obvious by the combination of Sollevi with Foster et al. Applicant contends that not all conditions which are characterized by platelet aggregation or thrombosis are associated with gpIIbIIIa. Applicant specifically argues that while other mechanisms for such conditions exist, the claims are directed only to

those conditions associated with inappropriate activity of the gpIIbIIIa receptor and Sollevi is silent with respect to this limitation. Applicant argues that Sollevi indicates that adenosine may inhibit clot formation and may inhibit platelet aggregation, but provides no indication that inhibition is due to the effect of adenosine on the receptor protein gpIIbIIIa since the thrust of Sollevi is that adenosine useful as a vasodilator.

In response, Sollevi at column 3, lines 12-15 teaches that adenosine **is** useful in inhibiting clot formations, and at column 20, lines 20-23 that adenosine **has** an inhibiting effect on platelet aggregation. Further, in response to Applicant's argument that Sollevi fails to teach that the inhibition is due to the effect of adenosine on gpIIbIIIa, Applicant fails to prove nor provide that the adenosine composition in the method of Sollevi or Wang did not function to inhibit platelet aggregation or thrombosis by way of inhibiting the activation of the platelet membrane receptor protein gpIIbIIIa. Absent evidence to the contrary, the adenosine administered to mammals, including humans in the method of Sollevi and Wang, effectively inhibited the activation of the platelet membrane receptor protein gpIIbIIIa, in order to inhibit platelet aggregation or thrombosis, as recited in the claimed invention.

9. No claims are allowed.

10. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
September 4, 2003

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/1641